# EXPERIMENTAL STUDIES ON ELECTIVE CARDIAC ARREST FOR OPEN HEART SURGERY

by

SADAAKI KAWASHIMA

From the lst. Surgical Division, Yamaguchi Medical School
(Director: Prof. Dr. AKIRA MATSUMOTO)
(Received for publication Nov. 6. 1958.)

## I INTRODUCTION

For any surgical procedure, it is ideal to obtain a motionless as well as bloodless operative field with good exposure. From this point of view, attempts to use artificially induced ventricular fibrillation or cardiac arrest as an adjunct for open heart surgery and then to resuscitate the heart by means of cardiac massage and countershock following the completion of intracradiac surgery were made, and it was reported that both adjuncts provide some advantages.[9)19)28)31)] However, SASAKI in our clinic,[27)] demonstrated that the clinical application of these techniques cannot be recommended on the basis of the experimental data, which revealed that the results of cardiac exclusion during ventricular fibrillation and cardiac arrest are worse than during sinus rhythm and cardiac resuscitation consisting of massage and coutershock, sometimes, produces serious myocardial damages such as fragmentation, hemorrhage, degeneration and necrosis.

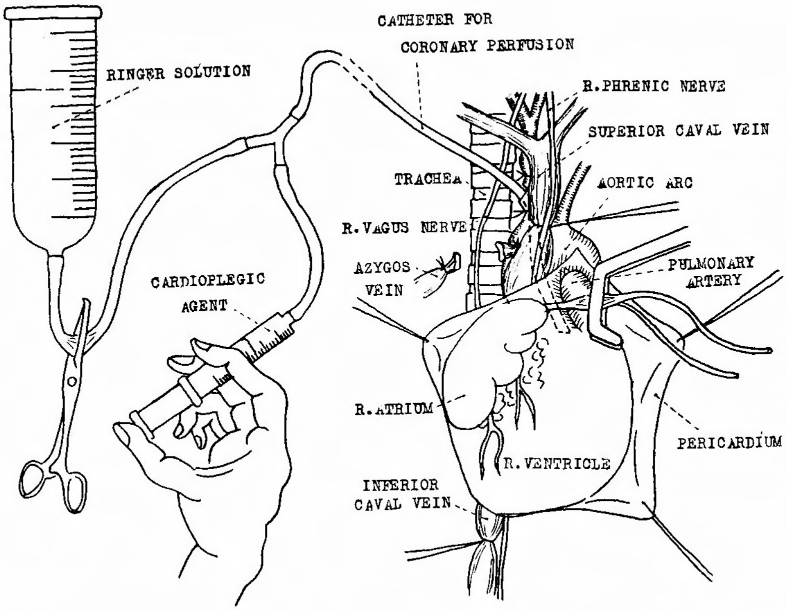
Recently, the attempt has been made to stop the heart with potassium citrate [3)6)7)8)11)16)22)] or acetylcholine[2)17)18)20)24)] during cardiac exclusion under hypothermia or extracorporeal circulation and then to restart it by reestablishing coronary perfusion with RINGER solution or blood to wash out potassium, or, by neutralizing intracoronary acetylcholine with atropine. Since EFFLER's success (1956), brilliant achievements have been brought about by this technique in the province of open heart surgery. However, it has not yet gained general acceptance. Theoretically, cardiac arrest seems to have obvious advantages. Would unforeseen difficulties arise with this new method? The present studies are concerned with this problem.

## II METHODS

### (1) *Elective Cardiac Arrest under Normo- and Hypothermia*

Healthy mongrel dogs weighing 6.5-17 kg, were anesthetized with pentobarbital (30-40 mg/kg). Lung inflation was maintained by intermittent positive pressure with pure oxygen through an endotracheal tube. Some animals were used under normothermia. The others were cooled by immersion in ice water except their heads until a rectal temperature of 30-32°C was obtained. After removal from the water bath the body temperature dropped further to 26-30°C, where it stabilized. With steril technique, the chest was entered through the right fourth intercostal space. After the azygos vein was cut between double ligatures, the brachiocephalic artery was completely isolated from the surrounding tissue under local anesthesia with 0.5% procain solution to prevent ventricular fibrillation due to vagal stimulation. The pericardium was widely opened parallel to the right phrenic nerve. A catheter filled with heparinized physiologic saline solution was introduced through an incision of the brachiocephalic artery into the ascending aorta for coronary perfusion of cardioplegic agent and RINGER solution, respectively, to stop and then to restart the heart (Fig. 1). The superior and inferior caval veins were occluded

**Fig. 1** Diagram Illustrating the Method of Stopping and Restarting the Heart



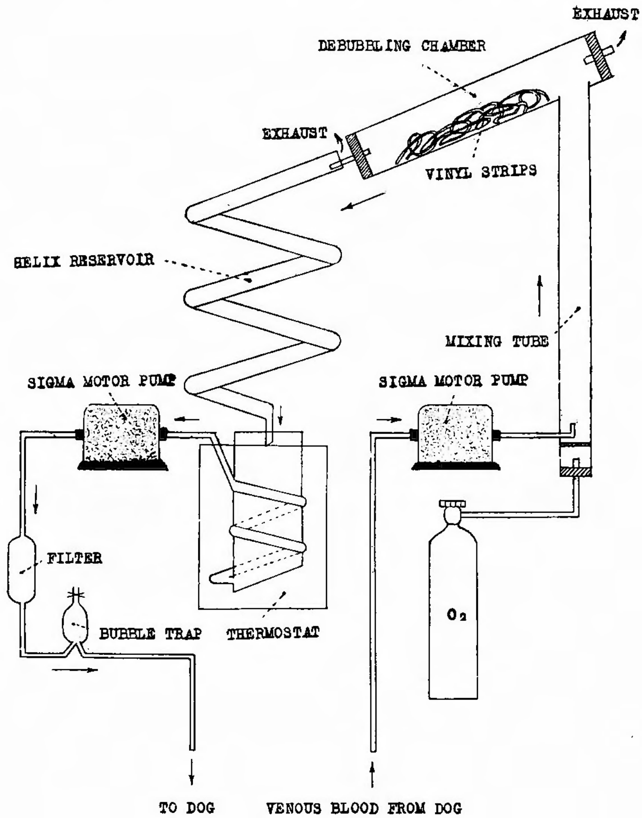

with tapes (inflow occlusion). After a few beats were allowed for cardiac emptying, the aorta and the pulmonary artery were at once occluded with a rubber cord passed through the transverse pericardial sinus over the catheter (outflow occlusion). Then cardioplegic agent was rapidly perfused until the heart was completely stopped. After cardiac arrest for five and fifteen minutes, respectively, in the normo- and hypothermic state, or, the formation and repair of ventricular septal defect during cardiac arrest under hypothermia had been performed, coronary perfusion of RINGER solution was instituted by gravity flow, under a difference of 90 cm in elevation. The perfused solution was aspirated through a right atrial or ventricular incision. In the second half of this study intermittent positive pressure breathing was not interrupted even during cardiac exclusion, in order to prevent complications, such as hemorrhagic atelectasis and hemothorax.

After restarting the heart, inflow occlusion was released so that bubbles were completely driven out from the opened heart by the blood which would pour into the cardiac cavity, and then the cardiotomy was sutured just prior to release of outflow occlusion. Blood was properly allowed to escape from the opened heart to avoid the over-dilatation of the right heart. When the heart did not regain sufficiently sinus rhythm, 1.0 cc of 1 : 10,000 epinephrine was injected into the left ventricle. The catheter in the ascending aorta was removed. The chest wall was firmly closed with two layers of suture after intrapleural application of penicillin crystal of 200,00 units. No drainage was practised.

(2) *Elective Cardiac Arrest with Extracorporeal Circulation*

Healthy mongrel dogs weighing 12–17 kg, were anesthetized exactly the same as before. A polyethylene catheter was placed in the femoral artery for direct measurement of arterial blood pressure by mercury manometer. Right thoracotomy was done. After the azygos vein was ligated, the venous cannulae were introduced into the superior and inferior venae cavae through separate stab wounds made in the right atrial wall. The arterial cannula was placed in the right carotid artery. Prior to cannulation, heparin of 2 mg per kilogram of weight was given intravenously for anticoagulation. A DeWall type bubble oxygenator and Sigmamotor pump apparatus were used.[4)5)21)] Thermostat was provided in the extracorporeal system to prevent cooling of blood (Fig. 2).

**Fig. 2** Diagram Illustrating Pump-oxygenator




For priming the heart-lung machine, the blood was obtained by bleeding hyperoxygenated normal dogs from the carotid artery under anesthesia with succinylcholin (20 mg for each dog subcutaneously), and collected in glass bottles containing 10 cc of 5% glucose mixed with 20 mg of heparin and 100,000 units of penicillin crystal per 1000 cc of blood.

Prior to extracorporeal circulation, cross-matchings of blood between donor and recipient and those between recipients were not performed on the basis of the following experimental data.

Forty dogs were divided into five groups and then in each group cross-matchings of blood were done within a few hours after getting blood (Table 1).

(i) In dogs, sometimes, hemagglutination took place so faint that it was difficult to decide whether it was positive or not.

(ii) Even if it was decided that it was one plus, the grade of agglutination was,

**TABLE 1.** Results of Cross Matchings of Canine Blood

| | | GROUP I (7) | II (7) | III (8) | IV (9) | V (9) | (40) |
|---|---|---|---|---|---|---|---|
| Hemagglutination | − | 22 | 30 | 15 | 49 | 45 | **161** |
| | ± | 1 | 0 | 2 | 11 | 4 | **18** |
| | + | 19 | 7 | 39 | 10 | 16 | **91** |
| | ++ | 0 | 5 | 0 | 2 | 7 | **14** |
| | | | | | | Total | **284** |

The figures in parenthesis show the number of dogs.

generally, far slighter than in man.

(iii) Out of 284 cross matchings, only 14 (5%) showed distinct hemagglutination (two plus), a sign which definitely rejects blood transfusion.

The animal was first on the pump-oxygenator "run" with gradually increasing flow (the 1st. partial perfusion). After flow and arterial pressure had been stabilized, inflow and then outflow occlusion were made. Injection of cardioplegic agent was rapidly performed with a syringe into the proximal aorta through its wall, where a purse string suture had been previously placed, and continued until the heart was stopped. The organs other than the heart were protected by extracorporeal circulation during cardiac arrest. After twenty minutes of cardiac arrest, the heart was restarted simply by releasing outflow occlusion and allowing coronary perfusion to resume with oxygenated blood. The blood having flowed into the cardiac cavity from the sinus was aspirated through a right atriotomy which was to be closed following the resumption of the heart beat. The inflow occlusion was released. Thus the 2 nd. partial perfusion was instituted. If the heart beat was effective, the pump-oxygenator "run" was discontinued for a trial period. If the heart was by itself able to maintain an adequate arterial pressure, the operation was terminated. As previously described, attempts to prevent pulmonary complications and over-dilatation of the right heart were made. To counteract the heparin effect, 3-4 mg per kilogram of protamine sulfate diluted in 20 cc of 5% glucose was slowly administered intravenously. The cannulae placed in both caval veins and the carotid artery were withdrawn. The chest wall was firmly closed after 200,000 units of penicillin crystal was applied in the pleural cavity, in which a rubber tube was left for drainage.

(3) *Histopathological Examinations on the Heart*

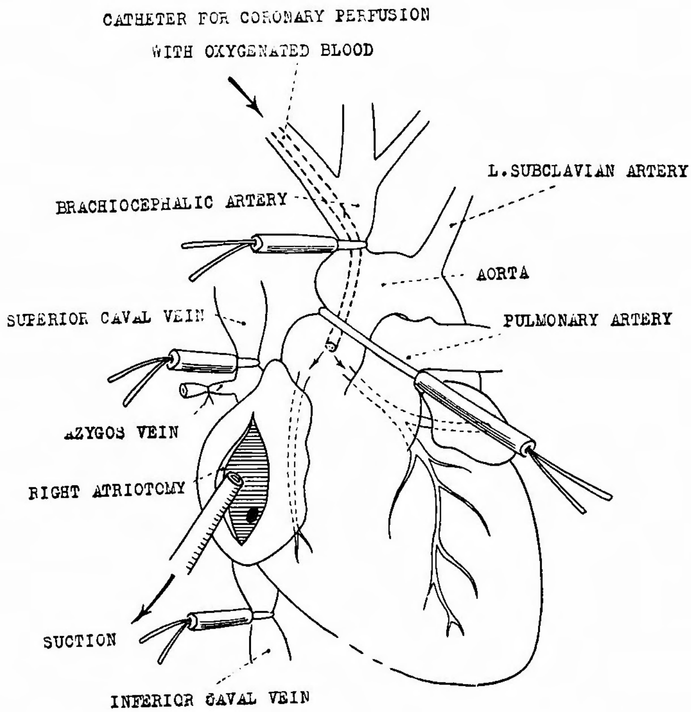
When the dogs survived, they were killed. Pieces of cardiac tissue were resected from both ventricular walls and the apex and then fixed in a 10% formalin solution. From each block, microscopical specimens stained with hematoxylin-eosin were made.

(4) *Cardiac Exclusion under Coronary Perfusion with Oxygenated Blood in Hypothermic State*

For comparison of the results of the above mentioned studies, this study was carried out.

In hypothermic dogs having a rectal temperature ranging from 25 to 27.8°C, the chest was entered through the right fourth intercostal space, and then a catheter for coronary perfusion was introduced via the right subclavian branch of the brachiocephalic artery into the ascending aorta (Fig. 3).

**Fig. 3,** Diagrammatic Illustration of the Method of Cardiac Exclusion during Sinus Rhythm with Coronary Perfusion of Oxygenated Blood




The blood for perfusion was obtained by bleeding normal dogs from the carotid artery, after they had been lightly anesthetized with pentobarbital. The blood was collected in glass bottles containing 29 mg of heparin per 1000 cc of blood and saturated by bubbling through it a jet of 100 per cent oxygen. Cross-matchings of blood were not undertaken.

Venous inflow occlusion was made at first. Snaring of the aorta over the catheter caused all of the blood to enter the coronary arteries by gravity flow under a difference of 1-2 m in elevation. During coronary perfusion, the blood flowing into the cardiac cavity from the sinus was allowed to escape through the opened heart.

After twenty minutes of cardiac exclusion, inflow occlusion was released, and then the cardiotomy was sutured prior to reopening the aorta, taking care to prevent air embolism. At the completion of the operation, protamine sulfate was not given. The chest wall was firmly closed. No drainage was practised.

## III RESULTS

(1) *Comparison of the Cardioplegic Effects of a 10% Solution of Potassium Chloride and "YOUNG Solution"*

The ideal cardioplegic agent for cardiac surgery should have the following characteristics: rapid and complete induction of cardiac arrest, rapid restoration of cardiac activity on re-establishment of coronary perfusion, absence of ventricular fibrillation, no occurrence of myocardial damage and lack of toxicity even if the entire cardioplegic dose was absorbed into general circulation.

A solution containing 0.54 g per cent potassium citrate and 2.47 g per cent magnesium sulfate is recommended by YOUNG et al.[23)33)] as an excellent solution for producing cardiac arrest, because these chemicals are more effective in combination than when used alone, due to their synergistic effects. Just prior to using this solution, small quantities of prostigmin (1 mg per 100 cc) are added. For convenience we call this mixture "YOUNG solution".

To compare the cardioplegic effects of a 10% KCl solution and "YOUNG solution", the heart in the normothermic state was stopped for 5 minutes with these solutions and was restarted by coronary perfusion with RINGER solution. An experiment using 18 dogs in all was carried out, in which one cardioplegic solution was used for 9 dogs, and the other solution used for the other 9 dogs.

(i) Cardiac Arrest Induced with Potassium Chloride Solution (Table 2, and Fig. 4)

**TABLE 2.** Results of Cardiac Arrest Induced with Ten per Cent Potassium Chloride for Five Minutes under Normothermia

| Dog No. | Weight (kg) | KCl Solution (cc) | | Restarting Heart | | Ventricular Fibrillation |
|---|---|---|---|---|---|---|
| | | Total | Per kg | RINGER Solution (cc) | Time (Sec.) | |
| 1 | 7.0 | 25 | 3.6 | 1200 | 240 | + |
| 2 | 8.0 | 15 | 1.9 | 800 | 630 | + |
| 9 | 11.0 | 10 | 0.9 | | | No recovery |
| 10 | 6.5 | 4 | 0.6 | 240 | 144 | + |
| 13 | 9.5 | 5 | 0.5 | 320 | 144 | − |
| 14 | 8.5 | 5 | 0.6 | 140 | 47 | − |
| 15 | 9.5 | 5 | 0.5 | 620 | 323 | − |
| 17 | 8.5 | 10 | 1.2 | 650 | 300 | + |
| 18 | 12.5 | 15 | 1.2 | 1200 | 260 | + |
| Mean | 9.0 | 10.4 | 1.2 | 646 | 261 | |

The amount of the cardioplegic solution perfused to stop the heart ranged from 4 to 25 cc (10.4 cc on the average), i. e., from 0.5 to 3.6 cc per kilogram (1.2 cc on the average). On coronary perfusion with RINGER solution, one of 9 animals did not regain the heart beat. The remaining 8 resumed the cardiac activity, but 5 of them had ventricular fibrillation after 20 seconds lasting up to 3 minutes. The time required to restart the heart ranged from 47 to 630 seconds (261 seconds on the average) and the amount of RINGER solution perfused to do

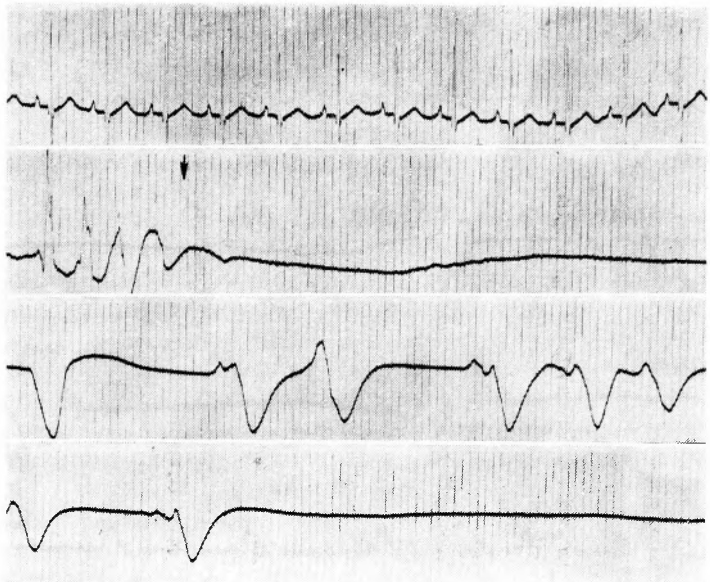


**Fig. 4.** Electrocardiographic tracings in Lead II made before, and after injection of a 10% KCl solution into the coronary circulation (dog No. 18). 1, Before injection. 2, Seven seconds after injection : the arrow points out the onset of cardiac arrest. 3, The heart was restarted 4 minutes after coronary perfusion with Ringer solution. 4, Cardiac arrest reappeared 40 seconds after recovery.

**TABLE 3.** Results of Cardiac Arrest Induced with "Young Solution" for Five Minutes under Normothermia

| Dog No. | Weight (kg) | Young Solution | | Restarting Heart | | Ventricular Fibrillation |
|---|---|---|---|---|---|---|
| | | Total | Per kg | Ringer Solution (cc) | Time (Sec.) | |
| 3 | 8.5 | 14 | 1.6 | 50 | 25 | — |
| 4 | 7.0 | 10 | 1.4 | 200 | 38 | — |
| 5 | 10.0 | 20 | 2.0 | 200 | 25 | — |
| 6 | 9.0 | 10 | 1.1 | 150 | 65 | — |
| 7 | 9.5 | 35 | 3.7 | 250 | 165 | — |
| 8 | 7.0 | 10 | 1.4 | 50 | 19 | — |
| 11 | 9.5 | 55 | 5.8 | 250 | 49 | — |
| 12 | 16.0 | 50 | 3.1 | 50 | 10 | — |
| 16 | 9.5 | 20 | 2.1 | 220 | 82 | — |
| Mean | 9.6 | 24.9 | 2.6 | 158 | 53 | |

so from 140 to 1200 cc (646 cc on the average).

(ii) Cardiac Arrest Induced with "Young Solution" (Table 3, and Fig. 5)

The amount of the cardioplegic solution perfused to stop the heart ranged from 10 to 55 cc (24.9 cc on the average), i. e., from 1.1 to 5.8 cc per kilogram (2.6 cc on the average). All 9 animals regained the heart beat. None of them had ventricular fibrillation thereafter. The time required to restart the heart ranged from 10 to 165 seconds (53 seconds on the average) and the amount of Ringer solution perfused to do so from 50 to 250 cc (158 cc on the average).

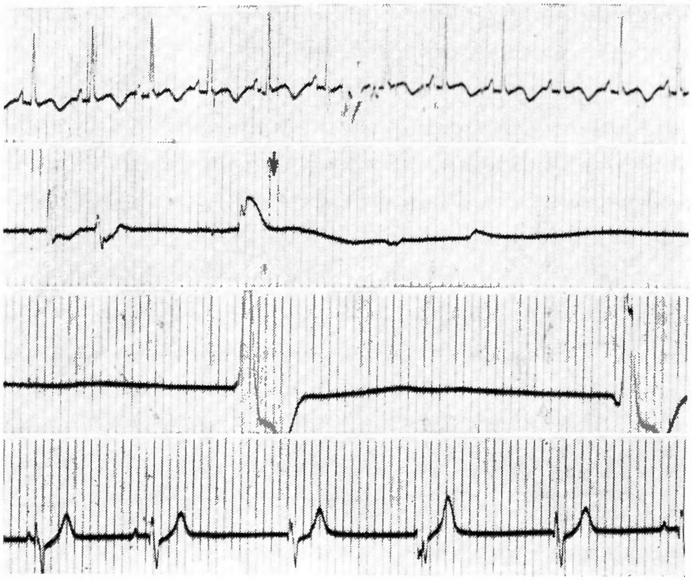


**Fig. 5.** Electrocardiographic tracings in Lead II made before, and after injection of "YOUNG solution" into the coronary circulation (dog No. 16). 1, Before injection. 2, Eleven seconds after injection : the arrow points out the onset of cardiac arrest. 3, The heart was restarted one minute and 22 seconds after coronary perfusion with RINGER solution. 4, Ten minutes after resumption of the heart beat.

In the group of "YOUNG solution", all animals resumed cardiac activity and thereafter had no ventricular fibrillation. On the contrary, only 3 of 9 cases in which the heart had been stopped with potassium chloride permanently regained the heart beat, 5 had ventricular fibrillation, after having made a transitory recovery, and one remained in the state of cardiac arrest. The hearts which had been stopped with "YOUNG solution" were far more rapidly restarted than those which had been stopped with potassium chloride, i. e., the time required to restart the former was, on the average, about one-fifth of the time required to restart the latter.

To sum up, "YOUNG solution" was, compared with the potassium chloride solution, found to be far more beneficial in regard to speed and completeness of recovery.

(2) *Cardiac Arrest Induced with "YOUNG solution" for Fifteen Minutes in Hypothermic State*

Hereafter, only "YOUNG solution" was used to stop the heart, because this solution had been found to be superior to the potassium chloride solution. Eighteen dogs were divided into 2 group of 9 each. In the second half of this study, the cardioplegic solution was aspirated as much as possible immediately after the heart had been completely stopped.

(i) Results in the First Half of the Study (Table 4)

The amount of "YOUNG solution" perfused to stop the heart ranged from 20 to 80 cc (43.9 cc on the average), i. e., from 2.3 to 5.2 per kilogram (3.6 cc on the

**TABLE 4.** Results of Cardiac Arrest Induced with "Young Solution" for Fifteen Minutes under Hypothermia in the First Half of the Study

| Dog No. | Weight (kg) | Young Solution (cc) | | Restarting Heart | | Ventricular Fibrillation | Time of Cardiac Exclusion (Min.) | Outcome |
|---|---|---|---|---|---|---|---|---|
| | | Total | Per kg | Ringer Solution (cc) | Time (Sec.) | | | |
| 19 | 7.5 | 20 | 2.7 | 580 | 323 | − | 21.6 | Died after 7 hours. |
| 20 | 8.5 | 40 | 4.7 | 260 | 95 | − | 16.8 | Died after 1 hour. |
| 21 | 16.0 | 40 | 2.5 | 120 | 23 | − | 16.3 | Killed after 10 days. |
| 22 | 10.5 | 30 | 2.9 | 280 | 53 | + | 16.2 | Died of ventricular fibrillation. |
| 23 | 13.0 | 30 | 2.3 | 220 | 63 | + | 17.2 | 〃 |
| 24 | 10.5 | 40 | 3.8 | 110 | 22 | − | 16.4 | Died after 5 days. |
| 25 | 15.5 | 80 | 5.2 | 80 | 25 | − | 17.0 | Died after 12 hours. |
| 26 | 15.0 | 70 | 4.7 | 220 | 52 | − | 17.0 | 〃 |
| Mean | 12.1 | 43.9 | 3.6 | 234 | 82 | | 17.3 | |

average). The time required to restart the heart ranged from 22 to 323 seconds (82 seconds on the average) and the amount of Ringer solution perfused to do so from 80 to 580 cc (234 cc on the average). The period of cardiac exclusion ranged from 16.2 to 21.6 minutes (17.3 minutes on the average).

In 2 of 8, ventricular fibrillation occurred following resumption of the heart beat, 10 and 16 minutes after, respectively. Cardiac resuscitation was not attempted. Four animals, after having made a good immediate recovery, died within 12 hours after surgery with hemothorax and hemorrhagic atelectasis. Only 2 survived, but one of them (No. 25) was killed in an accident 5 days after the operation.

**TABLE 5.** Results of Cardiac Arrest Induced with "Young Solution" for Fifteen Minutes under Hypothermia in the Second Half of the Study

| Dog No. | Weight (kg) | Young Solution (cc) | | Restarting Heart | | Ventricular Fibrillation | Time of Cardiac Exclusion (Min.) | Outcome |
|---|---|---|---|---|---|---|---|---|
| | | Total | Per Kg | Ringer Solution (cc) | Time (Sec.) | | | |
| 27 | 17.0 | 60–30 | 3.5–1.8 | 220 | 50 | — | 16.9 | Died after 3 days. |
| 28 | 7.0 | 20–10 | 2.8–1.4 | 100 | 25 | — | 16.4 | 〃 |
| 29 | 9.5 | 20–15 | 2.1–1.6 | 220 | 55 | — | 16.7 | Killed after 13 days. |
| 30 | 9.5 | 20–15 | 2.1–1.6 | 550 | 215 | — | 22.0 | Killed after 12 days. |
| 31 | 10.0 | 20–12 | 2.0–1.2 | 60 | 13 | — | 16.3 | Killed after 22 days. |
| 32 | 12.0 | 40–32 | 3.3–2.7 | 270 | 165 | — | 18.4 | Killed after 19 days. |
| 33 | 6.8 | 15–10 | 2.2–1.5 | 80 | 60 | — | 17.4 | Died after 6 days. |
| 34 | 6.0 | 15–10 | 2.5–1.7 | 160 | 100 | — | 17.4 | Died after 3 hours. |
| Mean | 9.7 | 26.3–16.8 | 2.7–1.8 | 208 | 85 | | 17.7 | |

In the second half of the study "Young solution" was reabsorbed as much as possible immediately after the onset of cardiac arrest. The minus figures show the amount of "Young solution" reabsorbed.

(ii) Results in the Second Half of the Study (Table 5)

The amount of "Young solution" perfused to stop the heart ranged from 15 to 60 cc (26.3 cc on the average), i. e., from 2 to 3.3 cc per kilogram (2.7 cc on the average), and the amount of this solution aspirated ranged from 10 to 30 cc (16.8 cc on the average), i. e., from 1.2 to 2.7 cc per kilogram (1.8 cc on the average).

The time recquired to restart the heart ranged from 25 to 215 seconds (85 second on the average), and the amount of Ringer solution perfused from 60 to 550 cc (208 cc on the average). The period of cardiac exclusion ranged from 16.3 to 22 minutes (17.7 minutes on the average).

In any dog, there was no ventricular fibrillation following resumption of the heart beat. Out of 8 animals, one died 3 hours after surgery, 3 died 3 to 6 days after with hemorrhagic atelectasis, and 4 survived.

The amount of "Young solution" per kilogram which was used in the second half of the study, was, on the average, three-fourths of that which was used in the first half. But the amount of Ringer solution perfused, and the time required to restart the heart were almost the same in each half.

The improvement in results was brought about by: a) the aspiration of as much of the cardioplegic solution as possible after stopping the heart; b) the prevention of the cardiac over-dilatation on the right side purposely by bleeding the heart from the atrial incision after release of inflow and outflow occlusions; c) the sufficient perfusion of Ringer solution until complete recovery of the heart, and d) balancing the amount of Ringer solution which was perfused

**TABLE 6.** Histological Findings of Myocardium Resulting from Cardiac Arrest Induced with "Young Solution" for Fifteen Minutes under Hypothermia

| Dog No. | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | | 30 | | 31 | | 32 | | 33 | | 34 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Time of Cardiac Exclusion (Min.) | 21.6 | | 16.8 | | 16.3 | | 16.2 | | 17.2 | | 16.4 | | 17.0 | | 17.0 | | 16.9 | | 16.4 | | 16.7 | | 22.0 | | 16.3 | | 18.4 | | 17.4 | | 17.4 | |
| Survival Period | 7 Hours | | 1 Hour | | 10 Days | | Immediate death | | Immediate death | | 5 Days | | 12 Hours | | 12 Hours | | 3 Days | | 3 Days | | 13 Days | | 12 Days | | 22 Days | | 19 Days | | 6 Days | | 3 Hours | |
| Heart | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R |
| Myocardium Degeneration | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Necrosis | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Interstitial Edema | - | - | + | - | - | - | - | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Perivascular Edema | - | - | + | - | - | - | - | - | - | - | + | + | - | - | - | - | - | - | - | - | + | - | + | + | - | - | - | - | - | - | - | - |
| Intimal Hyperplasia | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | + | + | - | - | + | - | - |
| Fragmentation | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Hemorrhage | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | + |
| Leucocyte Infitration | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

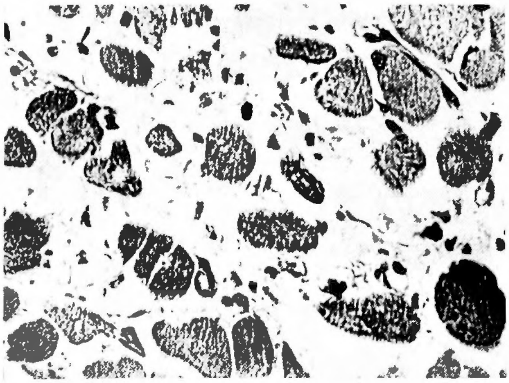


**Fig. 6.** Interstitial edema of myocardium, from dog No. 26, which was subjected to cardiac arrest induced with "Young solution" for 15 minutes under hypothermia and died 12 hours after operation.

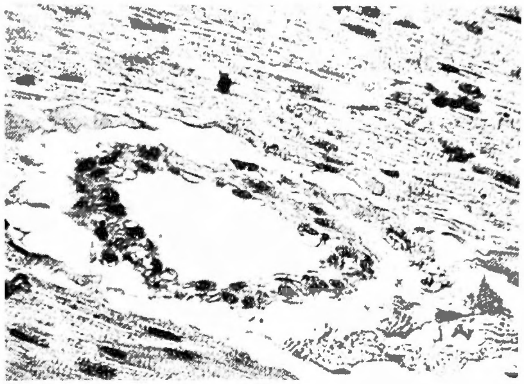


**Fig. 7.** Perivascular edema of myocardium, from dog No. 29, which was subjected to cardiac arrest induced with "Young solution" for 15 minutes under hypothermia and killed 13 days after operation.

**TABLE 7.** Results of Formation and Repair of Ventricular Septal Defect during Cardiac Arrest Induced with "YOUNG Solution" under Hypothermia

| Dog No. | Weight (kg) | Young Solution (cc) | | Restarting Heart | | Ventricular Fibrillation | Time of Cardiac Exclusion (Min.) | Outcome |
|---|---|---|---|---|---|---|---|---|
| | | Total | Per kg | Ringer Solution (cc) | Time (Sec.) | | | |
| 35* | 12.0 | 40– 5 | 3.3–0.4 | 80 | 155 | — | 13.0 | Killed after 14 days. |
| 36 | 15.5 | 60–35 | 3.9–2.2 | 40 | 15 | — | 11.8 | Killed after 12 days. |
| 37 | 12.0 | 30–25 | 2.5–2.1 | 250 | 100 | — | 7.3 | Died after 5 days. |
| 38* | 12.5 | 30–15 | 2.4–1.2 | 180 | 80 | — | 10.0 | Died after 16 hours. |
| 39 | 12.3 | 30–15 | 2.4–1.2 | 50 | 15 | — | 7.5 | Killed after 14 days. |
| 40 | 12.0 | 25– 0 | 1.1– 0 | 220 | 50 | — | 7.7 | Killed after 13 days. |
| 41 | 13.0 | 35–10 | 2.7–0.8 | 160 | 55 | — | 9.7 | Killed after 12 days. |
| 42* | 10.8 | 20–10 | 1.8–0.9 | 200 | 80 | — | 9.0 | Died after 12 hours. |
| 43* | 10.2 | 60–15 | 5.9–1.5 | 180 | 70 | — | 10.1 | Killed after 14 days. |
| 44* | 11.5 | 35–15 | 3.0–1.4 | 280 | 90 | — | 13.5 | Killed after 13 days. |
| Mean | 12.2 | 36.5–14.3 | 3.0–1.3 | 164 | 71 | | 9.9 | |

As in Table 5, the minus figures show the amount of "Young solution" reabsorbed. The cases marked with asterisks were injected with 1: 10,000 epinephrine into the left ventricle because of an insufficient recovery.

into the coronary arteries and that which was allowed to flow into the right atrium from the sinus, in order to prevent pulmonary edema which might to be caused by the solution flowing into the pulmonary veins beyond the aortic and mitral valves from the catheter in the ascending aorta.

If pulmonary edema had developed, tracheotomy was useful in curing it.

Histological examinations of all hearts subjected to this study revealed that there were found no myocardial degeneration and necrosis, but there was interstitial

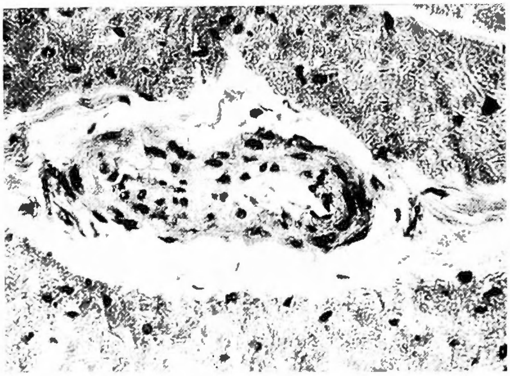


**Fig. 8.** Intimal hyperplasia of myocardium, from dog No. 32, which was subjected to cardiac arrest induced with "Young solution" for 15 minutes under hypothermia and killed 19 days after operation.

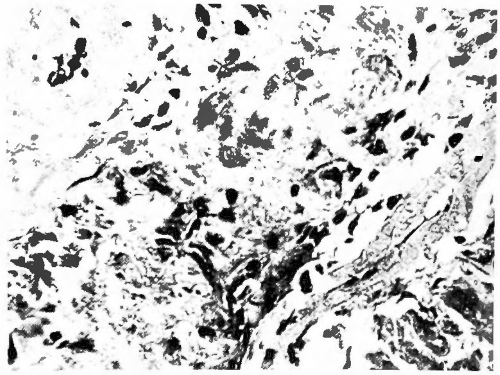


**Fig. 9.** Myocardial necrosis with granulocyte infiltration and calcification surrounded by degenerated muscle fibers in the cordial apex, from dog No. 36, which was killed 12 days after operation.

and perivascular edema, and intimal hyperplasia in a small number of dogs, perhaps due to coronary perfusion with Ringer and cardioplegic solutions (Table 6 and Fig. 6, 7 and 8).

3) *Formation and Repair of Ventriculal Septal Defect during Cardiac Arrest in Hypothermic State*

Ten dogs were used (Table 7). The heart was stopped with "Young solution" and delivered from the pericardial sac. About 4 cm of a right ventriculotomy was made. After sucking blood from the cardiac cavity, 1 to 2 cm of a superficial incision was made in the upper portion of the ventricular septum and then was penetrated into the left ventricular chamber by a tip of hemostat, where a small amount of the arterial blood gushed out from this wound. The defect was closed with a few interrupted sutures. At the completion of surgery the heart was restarted on coronary perfusion with Ringer solution.

The amount of "Young solution" required to stop the heart ranged from 20 to 60 cc (36.5 cc on the average), i. e., from 1.1 to 5.9 cc per kilogram (3.0 cc on the average), and the amount of the solution aspirated after stopping the heart from 0 to 35 cc (14.3 cc on the average), i. e., from 0 to 1.5 cc per kilogram (1.3 cc on the average). The time required to perform the intracardiac procedure ranged from 3.5 to 10.3 minutes (6.3 minutes on the average and the period of cardiac exclusion from 7.3 to 13.5 minutes (9.9 minutes on the average). The time required to restart the heart ranged from 15 to 155 seconds (71 seconds on the average), and the amount of Ringer solution perfused to do so from 40 to 280 cc (164 cc on the average).

None of 10 animals had ventricular fibrillation, after having regained the heart beat. Two died, 16 and 12 hours after operation, respectively, with hemorrhagic atelectasis. Eight survived. Thereafter one of them died of pyothorax 5 days following the surgery, after having made a good recovery.

The intracardiac procedure, the formation and repair of ventricular septal defect, was achieved easily, because the heart had been stopped in the atonic state.

**TABLE 8.** Histological Findings of Myocardium Resulting from Formation and Repair of Ventricular Septal Defect During Induced Cardiac Arrest under Hypothermia

| | Dog No. | 35 | | 36 | | 37 | | 38 | | 39 | | 40 | | 41 | | 42 | | 43 | | 44 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Time of Cadiac Exclusion (Min.) | 13.0 | | 11.8 | | 7.3 | | 10.0 | | 7.5 | | 7.7 | | 9.7 | | 9.0 | | 10.1 | | 13.5 | |
| | Survival Period | 14 Days | | 12 Days | | 5 Days | | 16 Hours | | 14 Days | | 13 Days | | 12 Days | | 12 Hours | | 14 Days | | 12 Days | |
| | Heart | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R | L | R |
| Myocardium | Degeneration | — | — | + | — | + | — | — | — | — | + | + | — | + | — | + | — | — | — | — | — |
| | Necrosis | — | — | + | + | + | — | — | — | ++ | ++ | + | — | — | — | — | — | — | — | — | — |
| | Interstitial Edema | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | Perivascular Edema | — | — | — | — | + | + | + | + | — | — | + | + | — | — | — | — | — | — | — | + |
| | Intimal Hyperplasia | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | Fragmentation | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | Hemorrhage | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | Leucocyte Infiltration | — | — | — | — | + | — | + | — | + | + | + | — | — | — | + | + | + | — | + | — |

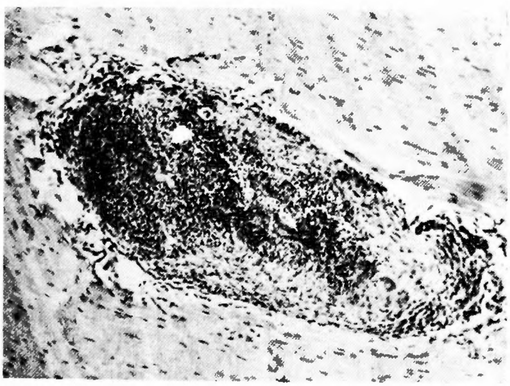


**Fig. 10.** Circumscribed myocardial necrosis with granulocyte infiltration surrounded by normal muscle fibers in the left ventricular wall, from the same dog as in Fig. 9.

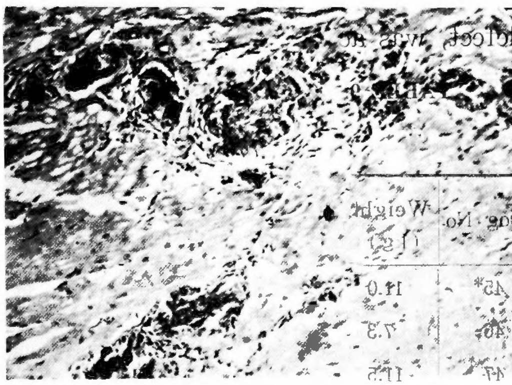


**Fig. 11.** Extensive myocardial necrosis with granulocyte infiltration and calcification accompanied by degenerated muscle fibers (vacuolization of protoplasm) in the right ventricular wall, from dog No. 39, which was killed 14 days after operation.

Histological examinations of the hearts subjected to this study revealed both myocardial necrosis and degeneration in 2 and only degeneration in 2 others, whereas in the remaining 6 the myocardium was almost normal (Table 8, and Fig. 9, 10, 11, 12, and 13).

(4) *Defibrillation by Stopping and then Restarting the Heart in Hypothermic State*

We happened to experience that the fibrillating heart can be stopped with "Young solution" and then converted into the normal rhythm by coronary perfusion with Ringer solution. This study was carried out to confirm such a matter (Table 9).

Ventricular fibrillation spontaneously developed in 2 animals during isolation of the brachiocephalic artery through which a catheter was to be introduced into the ascending aorta for coronary perfusion, and was electrically induced in 4

**Fig. 12.** Myocardial degeneration (pycnosis, loss of transverse striae and deeply stained protoplasm) in the left ventricular wall, from dog No. 41, which was killed 12 days after operation.

**Fig. 13.** Intermuscular hemorrhage with inflammatory reaction and myocardial degeneration (loss of transverse striae), from dog No. 42, which died 12 hours after operation.

defect, was achieved easily, because the heart had been stopped in the atonic state.

**TABLE 9.** Results of Defibrillation by Stopping and then Restarting the Heart on Coronary Perfusion with "YOUNG" and RINGER Solutions under Hypothermia

| Dog No. | Weight (kg) | Ventricular Fibrillation | | YOUNG Solution (cc) | | Restarting Heart | | Time of Cardiac Exclusion (Min.) | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| | | Modus | Duration (Sec.) | Total | Per kg | RINGER Solution cc | Time (Sec.) | | |
| 45* | 11.0 | Spontaneously | 10 | 25 | 2.3 | 80 | 15 | 7.4 | Killed after 10 days. |
| 46 | 7.3 | 〃 | 60 | 20–10 | 2.8–1.4 | 60 | 19 | 1.8 | Died after 2 days. |
| 47 | 11.5 | Electrically | 35 | 40–25 | 3.5–2.2 | 90 | 25 | 2.4 | Killed after 11 days. |
| 48 | 8.6 | 〃 | 40 | 50–30 | 5.8–3.5 | 120 | 40 | 2.6 | Died after 2 days. |
| 49 | 7.5 | 〃 | 30 | 45–20 | 6.0–2.7 | 60 | 15 | 2.1 | Killed after 10 days. |
| 50 | 8.2 | 〃 | 30 | 20– 5 | 2.4–0.6 | 70 | 30 | 3.0 | 〃 |
| Mean | 9.0 | 〃 | 34 | 33.0–15.0 | 3.8–2.1 | 80 | 24 | 3.2 | |

The case marked with an asterisk was subjected to cardiac massage.

The duration of fibrillation ranged from 10 to 60 seconds (34 seconds on the average), and the amount of "YOUNG solution" required to stop the fibrillating heart from 20 to 50 cc (33 cc on the average). In all animals, the heart was successfully resuscitated. The time required to restart the heart ranged from 15 to 40 seconds (24 seconds on the average), the amount of RINGER solution to do so from 60 to 120 cc (80 cc on the average), and the period of cardiac exclusion from 1.8 to 7.4 minutes (3.2 minutes on the average).

Four animals survived and 2 died, both 2 days after the operation, with hemorrhagic atelectasis.

(5) *Cardiac Exclusion for Twenty Minutes durings Sinus Rhythm with Coronary Perfusion of Oxygenated Blood under Hypothermia* (*Table* 10)

**TABLE 10.** Results of Cardiac Exclusion for Twenty Minutes during Sinus Rhythm with Coronary Perfusion of Oxygenated Blood under Hypothermia

| Dog No. | Weight (kg) | Perfused Blood (cc) | | Heart Beat | | Outcome |
|---|---|---|---|---|---|---|
| | | Total | Per kg Per Min | During Exclusion | After Release | |
| 101 | 7.0 | 800 | 5.7 | Rhythmical | Cardiac Arrest→Resuscitated→Cardiac Arrest | Died immediately. |
| 102* | 12.0 | 900 | 3.8 | Ventricular Fibrillation (just after)→Normal Beat on Perfusion | // | // |
| 103* | 11.5 | 980 | 3.7 | Rhythmical | Ventricular Fibrillation →Resuscitated | Died of pyothorax 5 days after. |
| 104 | 7.5 | 600 | 4.0 | Ventricular Fibrillation (6.5 min.) | Not resuscitated (hemoptysis due to pulmonary edema) | Died immediately. |
| 105* | 9.5 | 850 | 4.5 | Ventricular Fibrillation (18 min.) | Resuscitated | Died of Hemothorax 10 days after. |
| 106* | 9.5 | 500 | 2.6 | Ventricular Fibrillation (13.5 min.) | Resuscitated | Died of hemorrhagic atelectasis and hemothorax 2 days after. |

The animals marked with asterisks were injected with 1: 10,000 epinephrine into the left ventricle because of an incomplete recovery. All the hearts except one were resuscitated by means of cardiac massage and countershock.

The blood perfused ranged from 2.6 to 5.7 cc per kilogram per minute (4.1 cc on the average). In all cases, ventricular fibrillation and/or cardiac arrest occurred during cardiac exclusion or just after release of it. All the hearts but one were resuscitated by means of cardiac massage and countershock. Three of 6 cases died immediately after the operation. The remaining 3 died of complications such as hemothorax, hemorrhagic atelectasis and pyothorax within 10 days following the surgery, after having made a good recovery.

(6) *Cardiac Exclusion for Twenty Minutes during Cardiac Arrest Induced with "YOUNG solution" under Extracorporeal Circulation*

Six dogs were used in this study (Table 11). The amount of "YOUNG solution" required to stop the heart ranged from 16 to 60 cc (32.7 cc on the average), i. e., from 1.3 to 4.6 cc per kilogram (2.4 cc on the average).

In 5 cases, the heart beat was regained by re-establishing coronary circulation. The time required to restart the heart ranged from 9 to 50 seconds (42 seconds on the average). In one, ventricular fibrillation occurred just after release of outflow occlusion. Defibrillation was successfully achieved by means of cardiac massage and countershock.

Out of 6 animals, 2 survived, 2 died, 2.5 and 10 hours after the operation, respectively, and the remaining 2 both died 3 days following the surgery, after having made a good recovery. In these cases, the cause of death was profuse intrapleural hemorrhage.

The period of the lst. partial perfusion ranged from 1 to 4.9 minutes (2.9 minutes on the average), that of the total perfusion from 20.3 to 27.8 minutes (22.2 minutes on the average), and that of the 2nd. partial perfusion from 2.5 to 15.2 minutes (5.9 minutes on the average). The flow rate during total perfusion ranged from 47 to 81 cc per kilogram per minute.

The blood pressure was between 100 and 150 mm Hg before the operation. It ranged from 50 to 130 mm Hg during the 1st. partial perfusion, from 30 to 120 mm Hg during total perfusion and from 20 to 120 mm Hg during the 2nd. partial perfusion. At the completion of the surgery, it was between 60 and 120 mm Hg.

The pupils somewhat dilated in 4 of 6 cases during total perfusion, but returned to the initial size after this period. During extracorporeal circulation, the rectal temperature which had been between 38 and 39°C, fell in 2, respectively, by 0.5 and 1.0°C, remained unchanged in 2, and rose in one by 1.2°C.

Fig. 14 shows the course of operation in dog No. 203.

The histological findings of myocardium in the dogs undergoing this study were summarized in Table 12. Only in one of 6 cases, focal necrosis was found. In the others, except one (dog No. 204) in which severe subepicardial leucocyte infiltration in the right ventricular wall due to cardiac resuscitation (massage and countershock) was noted (Fig. 15), the myocardium was almost normal.

## IV DISCUSSION

*The Comparative Study of a Ten Per Cent Solution of Potassium Chloride and "YOUNG Solution".* —— This study was carried out with use of elective cardiac arrest for five minutes under normothermia. In five of nine animals having undergone cardiac arrest induced with potassium chloride,

**TABLE 11.** Results of Cardiac Exclusion for Twenty Minutes during Cardiac Arrest Induced with "YOUNG Solution" under Extracorporeal Circulation

| Dog No. | Weight (kg) | YOUNG Solution (cc) Total | YOUNG Solution (cc) Per kg | I Partial Perfusion: Blood Pressure (mmHg) | I Partial Perfusion: Rectal Temperature (°C) | I Partial Perfusion: Pupil Size (mm) | I Partial Perfusion: Duration (min) | Total Perfusion: Blood Pressure (mmHg) | Total Perfusion: Rectal Temperature (°C) | Total Perfusion: Pupil Size (mm) | Total Perfusion: Duration (min) | Total Perfusion: Flow cc/min/kg | II Partial Perfusion: Blood Pressure (mmHg) | II Partial Perfusion: Rectal Temperature (°C) | II Partial Perfusion: Pupil Size (mm) | II Partial Perfusion: Duration (min) | Ventricular Fibrillation | Time Required to Restart Heart (Min.) | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 203 | 12.4 | 40 | 3.2 | 120~130 | 38.0 | 3 | 2.0 | 80~120 | 37.4→36.8 | 2 | 20.3 | 61~81 | 40~90 | 36.5 | 2 | 5.8 | − | 21 | Killed after 14 days. |
| 204 | 13.2 | 30 | 2.1 | 80~120 | 37.5 | 2 | 1.0 | 80~100 | 37.5→37.0 | 2→4 | 27.8 | 57~76 | 30~100 | 37.5 | 4 | 3.4 | + | 420 | 〃 |
| 205 | 12.5 | 16 | 1.3 | 50~70 | 37.0 | 1→3 | 3.3 | 30~80 | 36.8→38.0 | 1→2 | 21.6 | 68~76 | 30~60 | 38.0 | 2→1 | 2.5 | − | 38 | Died after 3 days. |
| 206 | 13.0 | 60 | 4.6 | 75~100 | 38.0 | 1 | 3.0 | 30~60 | 37.5 | 1 | 21.5 | 55 | 20~60 | 37.5 | 2 | 5.5 | − | 90 | Died after 2.5 hours. |
| 207 | 16.7 | 28 | 1.7 | 120 | 39.0 | 2 | 4.9 | 40~70 | 38.0 | 2→3 | 20.9 | 47 | 60 | 38.0 | 2→1 | 3.2 | − | 50 | Died after 10 hours. |
| 208 | 15.5 | 22 | 1.4 | 90~110 | 39.0 | 1 | 3.3 | 70~90 | 38.5→37.0 | 1→2 | 21.0 | 77 | 40~120 | 37.0 | 2→1 | 15.2 | − | 9 | Died after 3 days. |

Dog No. 204 was resuscitated by means of cardiac massage and countershock.

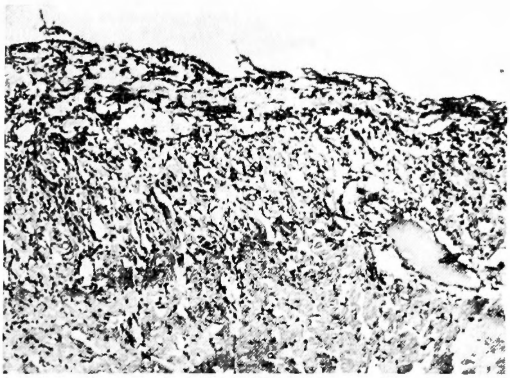


Fig. 15. Severe subepicardial leucocyte infiltration in the right ventricular wall, from dog No. 204 which was subjected to induced cardiac arrest for 20 minutes under extracorporeal circulation and then killed 14 days after the surgery. Cardiac resuscitation (massage and countershock) was successfully achieved.

ventricular fibrillation occurred during the recovery phase. In contrast, none of nine in the series using of "YOUNG solution" had such a complication. Moreover, the time required to restart the heart in the latter was on the average less than one-fifth of that in the former.

Consequently, as cardioplegic agent, "YOUNG solution" containing two components, potassium citrate and magnesium sulfate, is found to be superior to potassium chloride solution in regard to speed and completeness of recovery, and particularly in regard to the absence of troublesome complications such as ventricular fibrillation. This matter is brought about by the fact that synergists act more effectively and less harmfully when used in combination than when used alone.

The same principle is, generally, employed in combined anesthesia. In this point of view, combination of potassium citrate and acetylcholine is recommended.[12]

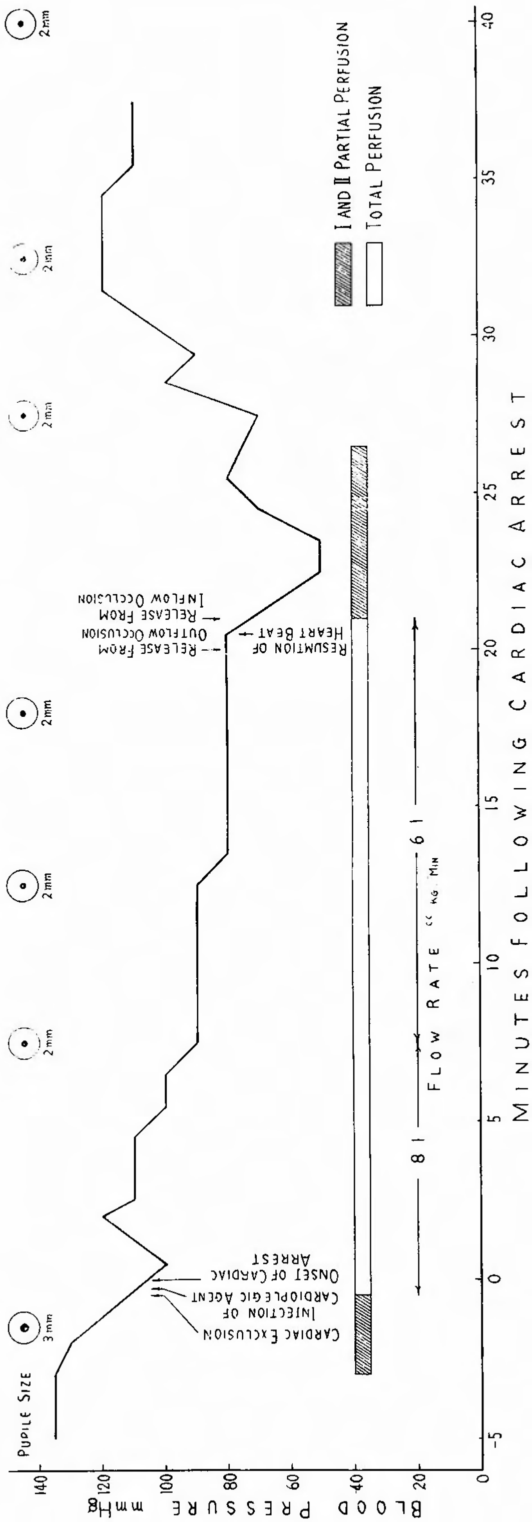



**Fig. 14.** Course of Induced Cardiac Arrest for Twenty Minutes under Extracorporeal Circulation (dog No. 203)

**TABLE 12.** Histological Findings of Myocardium Resulting from Induced Cardiac Arrest for Twenty Minutes under Extracorporeal Circulation

| | | 203 | | 204* | | 205 | | 206 | | 207 | | 208 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Time of cardiac Exclusion (Min) | | 20.3 | | 27.8 | | 21.6 | | 21.5 | | 20.9 | | 21.0 | |
| Survival Period | | 14 Days | | 14 Days | | 3 Days | | 2.5 Hours | | 10 Hours | | 3 Days | |
| Heart | | L | R | L | R | L | R | L | R | L | R | L | R |
| Myocardium | Degeneration | − | − | − | − | − | − | − | − | − | − | − | − |
| | Necrosis | + | − | ± | − | − | − | − | − | − | − | − | − |
| | Interstitial Edema | − | − | − | − | + | − | − | − | − | − | − | − |
| | Perivascular Edema | − | − | − | − | − | − | − | − | − | − | − | − |
| | Intimal Hyperplasia | − | − | − | − | − | − | − | − | − | − | − | − |
| | Fragmentation | − | − | − | − | − | − | − | − | − | − | − | − |
| | Hemorrhge | − | − | − | − | − | − | − | − | − | − | − | − |
| | Leucocyte Infiltration | + | − | − | ++ | − | − | − | − | − | − | − | − |

*… The dog was resuscitated by cardiac massage and countershock.

*Cardiac Arrest Induced with "YOUNG solution" for Fifteen Minutes under Hypothermia.*—In this study, only two of eighteen dogs had ventricular fibrillation during the recovery phase. This complication is apt to follow cardiac exclusion during sinus rhythm under hypothermia even with coronary perfusion of oxygenated blood. This matter will be discussed in detail.

According to MELROSE et al., the addition of stimulants, such as calcium chloride or adrenaline, is unnecessary and may be dangerous in resuscitating potassium arrest: spontaneous beating starts again usually with pure LOCK solution perfusion. Also, we used only RINGER solution with satisfactory results.

BERMAN et al.[1] demonstrated that quinidine given preoperatively decreases the incidence of ventricular fibrillation following cardiac arrest induced with acethylcholine in hypothermic dogs. This method seems to be worth trying.

As described under "Methods", there were many causes of improvement of the survival rate. The most important of these was the aspiration of the cardioplegic solution immediately after the induction of cardiac arrest. No fibrillation was encountered since having employed this technique. Consequently, the minimum quantity of cardioplegic agent should be used.

It was found that the right atrial pressure may rise to dangerously high levels when the heart is released from arrest. The over-distension of the right atrium is eliminated purposely by bleeding the heart from the right atriotomy prior to its complete closure.

During the recovery phase, a part of RINGER solution may flow back adversely into the pulmonary veins beyond the aortic and mitral valves, causing pulmonary edema. This complication can be prevented by maintaining the balance between the amount of RINGER solution perfused and that aspirated.

*Formation and Repair of Ventricular Septal Defect during Cardiac Arrest under Hypothermia.*—A completely motionless and bloodless operation field was obtained. The heart could be freely handled, particularly placing exact sutures when repairing the ventricular septal defect because of its complete flaccidity. In resuturing the cardiac wound, the elimination of coronary air embolism was almost counted for nothing. It is noticeable that none of ten animals having undergone the surgery had ventricular fibrillation in spite of direct manipulation of the heart. The operation was achieved quite easily and was followed by good results (an eighty per cent survival rate).

The one disadvantage incidental to this technique is that a certain time is required to restart the heart following completion of the operation. However, this period seems to be negligible, because it was, on the average, only one minute and eleven seconds.

*Crossmatching Donor and Recipient Dogs.*——The experiments of cardiac arrest with extracorporeal circulation and cardiac exclusion during sinus rhythm with coronary perfusion of oxygenated blood were carried out without regard for the possibility of blood incompatibility among dogs. We carried out 284 times of crossmatching according to SAKAUCHI and MATSUHASHI,[26] and round that five per cent of the tests showed distinct agglutination. (Suspicious and faint reactions were excluded.) HERMSWORTH et al.[13] reported that strong agglutination was noted in about twenty-five per cent of the examinations in which the recipients cells were matched with plasma from the prospective donors and replacement transfusion with the blood known to be incompatible caused renal ischemia and infarction, and severe pulmonary edema. SHOTSU[29] demonstrated that massive exchange of such blood is an important factor of postoperative bleeding.

Accordingly, there is little doubt that better results would be obtained if the determination of blood incompatibility had been carried out.

*Cardiac Exclusion during Sinus Rhythm for Twenty Minutes with Coronary Perfusion of Blood under Hypothermia.*——The coronary perfusion is carried out to prolong the safe period of cardiac exclusion and to avert ventricular fibrillation. However, troublesome complications occur frequently even with this technique.[10][15][25][30][32]

In all six animals subjected to this experiment, fibrillation and/or arrest occurred during exclusion or after release of it. With the exception of one, resuscitation was successfully achieved by means of massage and countershock. Nevertheless, there was no long-term survivor.

The causes of death were hemothorax, hemorrhagic atelectasis and pyothorax. Postoperative bleeding seemed to be due to perfusion of incompatible blood or no application of protamine sulfate.

The blood perfused ranging from 2.6 to 5.7 cc per kilogram per minute was adequate, judging from the experimental data reported by RIEERI et al..

*Induced Cardiac Arrest for Twenty Minutes with Extracorporeal Circulation.*——Perusal of the literature on extracorporeal circulation yielded a surprising variation in the reported flow rate (cc per kilogram per minute), i. e., GIBBON 83-124, KIRKLIN 50-80, KAY 40-80, LILLEHEI 26-60. In this study, the blood perfused during total perfusion ranged from 47 to 81 cc per kilogram per minute.

One of six animals had ventricular fibrillation during the recovery phase, but was resuscitated by means of massage and countershock. This animal was able to survive fairly well. Kolff et al. reported that a second arrest with potassium citrate is more effective procedure than electric shock to defibrillate the heart.

The cause of death in two animals which died three days after the surgery, was, in spite of postoperative application of protamine aulfate, profuse intrapleural hemorrhage perhaps due to incompatible blood transfusion. It is recommended by Kaplan et al.[14] that the left atrium cannulated and kept at normal pressure during potassium citrate cardiac arrest in order to remove the blood with a high potassium content in pulmonary circulation and to prevent postoperative complications, including pulmonary collapse and hemorrhage. Such a technique was not employed in the present study.

*Microscopical Examinations of Hearts.*——In the experiments of cardiac arrest induced with "Young solution" for fifteen minutes under hypothermia, there were found no myocardial degeneration or necrosis, but interstitial and perivascular edema, and intimal hyperplasia in a small number of dogs. These histological changes are supposed to result from coronary perfusion of the cardioplegic agent and Ringer solution.

In six of ten hearts subjected to the formation and repair of ventricular septal defect during cardiac arrest under hypothermia, the myocardium was almost normal and in the remaining four, degeneration and/or necrosis perhaps due to incidental trauma were found.

Cardiac exclusion during induced arrest for twenty minutes with extracorporeal circulation did not cause any histological change of the myocardium in the large majority of animals. On the other hand, it is known that only four to six minutes of inflow and outflow occlusion, if carried out under normothermia, will result in moderate myocardial damage. Consequently, it may be said from the histological point of view, that twenty minutes of cardiac exclusion under such circumstances is within the safe time limit. Kolff demonstrated that a dog's heart will resume a sinus rhythm after three hours of arrest. It is of interest to know this maximum safe time.

*Defibrillation by Induced Cardiac Arrest.*——As described already, defebrillation was successfully achieved by stopping and then restarting the heart with coronary perfusion of, respectively, cardioplegic agent and Ringer solution. This technique is of practical use in regard to absence of ill effect on the heart, even though it does not act as promptly as the resuscitation consisting of massage and countershock which may produce severe myocardial damage.

## V SUMMARY

(1) The present studies have been carried out to know whether elective cardiac arrest can be an useful adjunct to open heart surgery.

(2) In dogs, a catheter was introduced through the brachiocephalic artery into the ascending aorta for coronary perfusion of cardioplegic agent and Ringer solution, respectively, to stop and then restart the heart.

(i) To compare the cardioplegic effects of 10% potassium chloride and a

solution containing 2.47 Gm per cent magnesium fulfate and 0.54 Gm per cent potassinm citrate (YOUNG solution), the heart in the normothermic state was stopped with these solutions for 5 minutes and then restarted. The latter proved to be more beneficial in regard to speed and completeness of recovery, as well as causing no provocation of ventricular fibrillation.

(ii) In hypothermic dogs, cardiac arrest for 15 minutes was induced with "YOUNG solution" and followed by resuscitation. In the first half of the experiments, only 2 of 8 animals, but in the second, 7 of 8 survived. The improvement was brought about by: a) the aspiration of as much of the cardioplegic solution as possible after stopping the heart; b) the prevention of the over-distension of the right atrium by purposely bleeding the heart from the atrial incidion; c) the sufficient perfusion of RINGER solution until the accomplishment of a complete recovery, and d) the prevention of pulmonary edema which might be caused by RINGER solution flowing back into the pulmonary veins beyond the aortic and mitral valves from the catheter in the aorta.

In no case was there found myocardial degeneration or necrosis, but in a few, interstitial and perivascular edema and intimal hyperplasia.

(iii) Under hypothermia, the formation and repair of ventricular septal defect during induced cardiac arrest was achieved easily and with excellent results. No ventricular fibrillation was encountered. Histologically myocardial degeneration and necrosis were found only in a small number of animals.

(iv) Defibrillation was successfully achieved by stopping and then restarting the heart with coronary perfusion of, respectively, cardioplegic agent and RINGER solution. This technique, which produces no myocardial damage, is of practical use.

(3) For comparison, the experiments of cardiac exclusion for 20 minutes with coronary perfusion of oxygenated blood under hypothermia were carried out. In all animals, ventricular fibrillation occurred during exclusion or after release of it. The results were poor.

(4) Under extracorporeal circulation, the heart was excluded during induced cardiac arrest for 20 minutes and then restarted by re-establishment of coronary circulation. In only one of 6 animals, ventricular fibrillation developed. On histological examination, the myocardium was normal in almost all animals.

I am greatly indebted to Assist. Prof. Dr. RIKIO YAMAKI of our clinic for his constant, kind guidance during the course of the present studies.

An abstract of this article has been reported by Dr. YAMAKI at the 11th Annual Meeting of the Japanese Association for Thoracic Surgery on Sept. 26, 1958.

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## 和文抄録

# 直視下心内手術に於ける任意心搏停止の応用に関する実験的研究

山口県立医科大学外科学教室第1講座（主任：松本　彰教授）

川　島　貞　昭

1. 任意心搏停止が直視下心内手術に於て有用な補助手段であるかどうかを実験的に検討した．

2. 犬を用い腕頭動脈より大動脈起始部までポリエチレン管を挿入しInflow-Outflow閉鎖後直にこれより心搏停止剤を冠動脈内に注入して心搏停止を起こさしめ，一定の時間後或は心内操作終了後リンゲル氏液の冠灌流によつて心蘇生を行つた．

i) 心搏停止剤として10% KCl溶液と2.47Gm硫酸マグネシウム及び0.54 Gm%クエン酸カリの混合溶液（Young氏液）を用い，常温下5分間の任意心搏停止実験により両者を比較した．心蘇生の迅速なこと，心室細動を誘発しないことに於てYoung氏液が遙かに優れている．

ii) 全身冷却犬に対しYoung氏液を用い15分間の任意心搏停止実験を行つた．実験の前半期では8例中僅か2例が生存したが後半期では8例中7例が生存した．改善の原因は心搏停止後直に注入された心搏停止剤を吸引排除したこと，心搏再開後心房切開創を完全に閉鎖するに先立ち漸時出血せしめ右房の拡張を防止したこと，完全に心搏が再開するまで充分リンゲル氏液の冠灌流を行つたこと，リンゲル氏液の冠灌流に際しこれが大動脈弁更に僧帽弁を逆流し肺静脈に流入して起こる肺浮腫の予防に留意したことである．組織学的には少数例に心筋の間質及び血管周囲浮腫，動脈内膜肥厚を認めた．大多数例では心筋は正常であつた．

iii) 全身冷却犬を用いYoung氏液による任意心搏停止下に心室中隔欠損作成並に閉鎖実験を行つた．手術は容易で結果良好であつた．心室細動を起こした例は1例もなく，極く少数例に心筋の変性壊死が見られたに過ぎない．

iv) 任意心搏停止下にリンゲル氏液の冠灌流による心搏再開は心室細動除去に利用できる．本法は心筋を障害しないので臨床的応用の価値があると思われる．

3. 以上の実験と比較するために全身冷却犬で酸素加血冠灌流下に20分間心血流遮断を行つた．全例に心血流遮断中或は遮断解除後心室細動を発生し結果は不良であつた．

4. 体外循環下にYoung氏液を用い20分間の心搏停止実験を行い，冠血流の再開により心蘇生を行つた．6例中1例に心室細動が発生した．殆ど全例に於て心筋は正常像を示した．